

10/031786

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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International Bureau



(43) International Publication Date  
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number  
**WO 01/07651 A3**

- (51) International Patent Classification<sup>7</sup>: C12Q 1/68. C12N 15/10
- (21) International Application Number: PCT/GB00/02879
- (22) International Filing Date: 26 July 2000 (26.07.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
9917531.7 26 July 1999 (26.07.1999) GB
- (71) Applicant (for all designated States except US): **ARROW THERAPEUTICS LIMITED** [GB/GB]; Britannia House, 7 Trinity Street, London SE1 1DA (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **CHARLES, Ian, George** [GB/GB]; Arrow Therapeutics Limited, Britannia House, 7 Trinity Street, London SE1 1DA (GB). **MASKELL, Duncan, John** [GB/GB]; Centre for Veterinary Science, Department of Clinical Veterinary Medicine, University of Cambridge, Madingley Road, Cambridge CB3 0ES (GB).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
2 May 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 01/07651 A3

(54) Title: TRANSPOSON MEDIATED DIFFERENTIAL HYBRIDISATION

(57) Abstract: A method for identifying an essential gene of an organism comprises: (i) providing a library of transposon mutants of the said organism; (ii) isolating polynucleotide sequences from the library which flank inserted transposons; (iii) hybridising the said polynucleotide sequences with a polynucleotide library from the said organism; and (iv) identifying a polynucleotide in the said polynucleotide library to which the said polynucleotide sequences do not hybridise, thereby to determine an essential gene of the organism.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 00/02879

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 C12N15/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 20161 A (DEBOUCK CHRISTINE MARIE ;SMITHKLINE BEECHAM CORP (US); MOONEY JEFF) 14 May 1998 (1998-05-14) claims 1-22 page 2, line 12 -page 4, line 9 ---	1-10
X	CHUN K T ET AL: "THE IDENTIFICATION OF TRANSPOSON-TAGGED MUTATIONS IN ESSENTIAL GENES THAT AFFECT CELL MORPHOLOGY IN SACCHAROMYCES CEREVISIAE" GENETICS, GENETICS SOCIETY OF AMERICA, AUSTIN, TX, US, vol. 142, no. 1, January 1996 (1996-01), pages 39-50, XP000995589 ISSN: 0016-6731 page 40 -page 42 --- -/--	1,3,8



Further documents are listed in the continuation of box C



Patent family members are listed in annex

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

30 November 2001

Date of mailing of the international search report

06/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

van Klompenburg, W

# INTERNATIONAL SEARCH REPORT

In' tional Application No

PCT/GB 00/02879

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NELSON K E ET AL: "IDENTIFICATION OF THE MINIMAL ESSENTIAL GENE SET OF HAEMOPHILUS INFLUENZAE VIA TRANSPOSON MUTAGENESIS" ABSTRACTS OF THE GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, US, vol. 97, 4 May 1997 (1997-05-04), page 321 XP000994943 ISSN: 0067-2777 abstract	1,3
X	US 5 733 760 A (KILLEEN KEVIN ET AL) 31 March 1998 (1998-03-31) column 4, line 33 - line 63 column 8, line 33 - line 64 claims 1-13; figures 4,5	24-28
E	US 6 232 074 B1 (DAWSON DEAN ET AL) 15 May 2001 (2001-05-15) the whole document	1-3,10

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11-22

Present claims 11-22 relate to a compound defined by reference to a desirable characteristic or property, namely inhibiting transcription and/or translation of an essential or conditional essential gene.

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search of the claimed scope impossible. Consequently, no search has been carried out for those claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

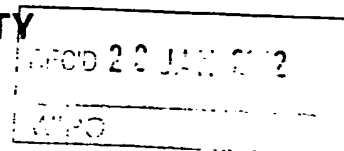
In tional Application No

PCT/GB 00/02879

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9820161	A	14-05-1998	EP 0948646 A1 JP 2001505417 T WO 9820161 A1	13-10-1999 24-04-2001 14-05-1998
US 5733760	A	31-03-1998	NONE	
US 6232074	B1	15-05-2001	AU 2074601 A WO 0142446 A2	18-06-2001 14-06-2001

# PATENT COOPERATION TREATY

## PCT



### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>N.76036A GCW</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/GB00/02879</b>	International filing date (day/month/year) <b>26/07/2000</b>	Priority date (day/month/year) <b>26/07/1999</b>
International Patent Classification (IPC) or national classification and IPC <b>C12Q1/68</b>		
Applicant <b>ARROW THERAPEUTICS LIMITED et al.</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand <b>31/01/2001</b>	Date of completion of this report <b>24.01.2002</b>
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer <b>Wieser, M</b> Telephone No. +49 89 2399 8434 

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02879

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-35 as originally filed

**Claims, No.:**

1-28 as originally filed

**Drawings, sheets:**

1/5-5/5 as originally filed

**Sequence listing part of the description, pages:**

32,34, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02879

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
- (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

### III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application.
  - ☒ claims Nos. 11-22.

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
  - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  - ☒ no international search report has been established for the said claims Nos. 11-22.
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the standard.
  - ☐ the computer readable form has not been furnished or does not comply with the standard.

### V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02879

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## 1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-10,23-28
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10,23-28
Industrial applicability (IA)	Yes:	Claims	1-10,23-28
	No:	Claims	

## 2. Citations and explanations see separate sheet

### **Section III**

Claims relating to inventions in respect of which no International Search Report has been established need not to be the subject of International Preliminary Examination (Rule 66(1)(e) PCT. Accordingly, claims 11-22 which are identified in the International Search Report as not having been searched, are not subject of this Report.

### **Section V**

D1: WO 98 20161 A (DEBOUCK CHRISTINE MARIE ;SMITHKLINE BEECHAM CORP (US); MOONEY JEFF) 14 May 1998 (1998-05-14)

D2: CHUN K T ET AL: 'THE IDENTIFICATION OF TRANSPOSON-TAGGED MUTATIONS IN ESSENTIAL GENES THAT AFFECT CELL MORPHOLOGY IN SACCHAROMYCES CEREVISIAE' GENETICS, GENETICS SOCIETY OF AMERICA, AUSTIN, TX, US, vol. 142, no. 1, January 1996 (1996-01), pages 39-50, XP000995589 ISSN: 0016-6731

D3: NELSON K E ET AL: 'IDENTIFICATION OF THE MINIMAL ESSENTIAL GENE SET OF HAEMOPHILUS INFLUENZAE VIA TRANSPOSON MUTAGENESIS' ABSTRACTS OF THE GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, US, vol. 97, 4 May 1997 (1997-05-04), page 321 XP000994943 ISSN: 0067-2777

D4: US-A-5 733 760 (KILLEEN KEVIN ET AL) 31 March 1998 (1998-03-31)

1. The problem underlying the present application is the need to for a method to identify essential and conditionally essential genes. According to the description this is solved by providing a method, wherein a transposon mutant library is created and screened by hybridisation with an array.

According to the broad and unspecific wording of the claims, the subject-matter of claims 1-10 and 23 is anticipated by the disclosure in D1 (see claims 1-22; and pages 2-4). The subject-matter of claims 1,3 and 8 is moreover anticipated by D2 (see pages 40-42), while D3 (abstract) takes away novelty from claims 1 and 3.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB00/02879

2. Claims 28-28 refer to a product, respectively its use, defined by a process for its production. Since such product cannot be differentiated from the prior art by a reference to its production, any bacterium attenuated by transposon mutagenesis falls under the scope of these claims. Accordingly, D4 (see claims 1-13, figures 4 and 5, ad columns 4 and 8) anticipates the novelty of these claims.
3. Consequently, claims 1-10 and 23-28 do not meet the requirements of Article 33(2) PCT.

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

WOODS, Geoffrey, Corlett  
J.A. Kemp & Co.  
14 South Square  
Gray's Inn  
London WC1R 5LX  
ROYAUME-UNI

Date of mailing (day/month/year) 07 February 2002 (07.02.02)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference N.76036A GCW	
International application No. PCT/GB00/02879	International filing date (day/month/year) 26 July 2000 (26.07.00)

1. The following indications appeared on record concerning:

☒ the applicant    ☐ the inventor    ☐ the agent    ☐ the common representative

Name and Address ARROW THERAPEUTICS LIMITED Woodmansterne Road Carshalton Surrey SM5 4DS United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person    ☐ the name    ☒ the address    ☐ the nationality    ☐ the residence

Name and Address ARROW THERAPEUTICS LIMITED Britannia House 7 Trinity Street London SE1 1DA United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office    ☐ the designated Offices concerned  
☐ the International Searching Authority    ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority    ☐ other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer R. Chrem Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

Date of mailing (day/month/year) 28 March 2001 (28.03.01)	
International application No. PCT/GB00/02879	Applicant's or agent's file reference N.76036A GCW
International filing date (day/month/year) 26 July 2000 (26.07.00)	Priority date (day/month/year) 26 July 1999 (26.07.99)
Applicant CHARLES, Ian, George et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
31 January 2001 (31.01.01)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Olivia TEFY
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

WOODS, Geoffrey, Corlett  
J.A. Kemp & Co.  
14 South Square  
Gray's Inn  
London WC1R 5LX  
ROYAUME-UNI

Date of mailing (day/month/year) 07 February 2002 (07.02.02)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference N.76036A GCW	
International application No. PCT/GB00/02879	International filing date (day/month/year) 26 July 2000 (26.07.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address CHARLES, Ian, George The Wolfson Institute for Biomedical Research The Cruciform Building University College London Gower Street London WC1E 6BT United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address CHARLES, Ian, George Arrow Therapeutics Limited Britannia House 7 Trinity Street London SE1 1DA United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer R. Chrem
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>N.76036A GCW</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 00/ 02879</b>	International filing date (day/month/year) <b>26/07/2000</b>	(Earliest) Priority Date (day/month/year) <b>26/07/1999</b>
Applicant <b>ARROW THERAPEUTICS LIMITED</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02879

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NELSON K E ET AL: "IDENTIFICATION OF THE MINIMAL ESSENTIAL GENE SET OF HAEMOPHILUS INFLUENZAE VIA TRANSPOSON MUTAGENESIS" ABSTRACTS OF THE GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, US, vol. 97, 4 May 1997 (1997-05-04), page 321 XP000994943 ISSN: 0067-2777 abstract ----	1,3
X	US 5 733 760 A (KILLEEN KEVIN ET AL) 31 March 1998 (1998-03-31) column 4, line 33 - line 63 column 8, line 33 - line 64 claims 1-13; figures 4,5 ----	24-28
E	US 6 232 074 B1 (DAWSON DEAN ET AL) 15 May 2001 (2001-05-15) the whole document -----	1-3,10



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/02879

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9820161	A	14-05-1998	EP 0948646 A1 JP 2001505417 T WO 9820161 A1	13-10-1999 24-04-2001 14-05-1998
US 5733760	A	31-03-1998	NONE	
US 6232074	B1	15-05-2001	AU 2074601 A WO 0142446 A2	18-06-2001 14-06-2001

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11-22

Present claims 11-22 relate to a compound defined by reference to a desirable characteristic or property, namely inhibiting transcription and/or translation of an essential or conditional essential gene.

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search of the claimed scope impossible. Consequently, no search has been carried out for those claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

International Application No

P GB 00/02879

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 C12Q1/68 C12N15/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 20161 A (DEBOUCK CHRISTINE MARIE ;SMITHKLINE BEECHAM CORP (US); MOONEY JEFF) 14 May 1998 (1998-05-14) claims 1-22 page 2, line 12 -page 4, line 9 ---	1-10
X	CHUN K T ET AL: "THE IDENTIFICATION OF TRANSPOSON-TAGGED MUTATIONS IN ESSENTIAL GENES THAT AFFECT CELL MORPHOLOGY IN SACCHAROMYCES CEREVISIAE" GENETICS, GENETICS SOCIETY OF AMERICA, AUSTIN, TX, US, vol. 142, no. 1, January 1996 (1996-01), pages 39-50, XP000995589 ISSN: 0016-6731 page 40 -page 42 --- -/--	1,3,8

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

30 November 2001

Date of mailing of the international search report

06/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

van Klompenburg, W

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

# PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

To:

J.A. KEMP & CO.  
Attn. WOODS, G.  
14 South Square  
Gray's Inn  
London WC1R 5LX  
UNITED KINGDOM

**J.A. KEMP & Co.**

Rec'd. 10 DEC 2001

Action by.....

Date of mailing  
(day/month/year)

06/12/2001

Applicant's or agent's file reference

N.76036A GCW

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/GB 00/02879

International filing date

(day/month/year)

26/07/2000

Applicant

ARROW THERAPEUTICS LIMITED

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Brigitta Klág

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

**"Statement under article 19(1)" (Rule 46.4)**

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

**Consequence if a demand for international preliminary examination has already been filed**

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

**Consequence with regard to translation of the international application for entry into the national phase**

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>N.76036A GCW</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 00/ 02879</b>	International filing date (day/month/year) <b>26/07/2000</b>	(Earliest) Priority Date (day/month/year) <b>26/07/1999</b>
Applicant  <b>ARROW THERAPEUTICS LIMITED</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02879

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 C12Q1/68 C12N15/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12Q C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 20161 A (DEBOUCK CHRISTINE MARIE ; SMITHKLINE BEECHAM CORP (US); MOONEY JEFF) 14 May 1998 (1998-05-14) claims 1-22 page 2, line 12 -page 4, line 9 ---	1-10
X	CHUN K T ET AL: "THE IDENTIFICATION OF TRANSPOSON-TAGGED MUTATIONS IN ESSENTIAL GENES THAT AFFECT CELL MORPHOLOGY IN SACCHAROMYCES CEREVISIAE" GENETICS, GENETICS SOCIETY OF AMERICA, AUSTIN, TX, US, vol. 142, no. 1, January 1996 (1996-01), pages 39-50, XP000995589 ISSN: 0016-6731 page 40 -page 42 ----- -/--	1,3,8



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*S\* document member of the same patent family

Date of the actual completion of the international search

30 November 2001

Date of mailing of the international search report

06/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

van Klompenburg, W



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02879

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NELSON K E ET AL: "IDENTIFICATION OF THE MINIMAL ESSENTIAL GENE SET OF HAEMOPHILUS INFLUENZAE VIA TRANSPOSON MUTAGENESIS" ABSTRACTS OF THE GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, US, vol. 97, 4 May 1997 (1997-05-04), page 321 XP000994943 ISSN: 0067-2777 abstract ----	1,3
X	US 5 733 760 A (KILLEEN KEVIN ET AL) 31 March 1998 (1998-03-31) column 4, line 33 - line 63 column 8, line 33 - line 64 claims 1-13; figures 4,5 ----	24-28
E	US 6 232 074 B1 (DAWSON DEAN ET AL) 15 May 2001 (2001-05-15) the whole document -----	1-3,10

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11-22

Present claims 11-22 relate to a compound defined by reference to a desirable characteristic or property, namely inhibiting transcription and/or translation of an essential or conditional essential gene.

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search of the claimed scope impossible. Consequently, no search has been carried out for those claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 00/02879

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claim 28 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 11-22  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/02879

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9820161	A	14-05-1998	EP 0948646 A1 JP 2001505417 T WO 9820161 A1	13-10-1999 24-04-2001 14-05-1998
US 5733760	A	31-03-1998	NONE	
US 6232074	B1	15-05-2001	AU 2074601 A WO 0142446 A2	18-06-2001 14-06-2001